some genes for psychosis could be controlled by sex-linked factors and produce various types of concordance. Muscular dystrophy in man not only has allelic types of varying severity located on Xp21, but also there are autosomal loci with similar phenotype (McKusick, 1988). So it is by no means impossible that one phenotype can be produced by several loci or a single locus with multiple alleles. Thus, the question of heterogeneity must not be forgotten. There is already experimental evidence for it (*Lancet*, 1987, 1988), but in a previous communication Dr Crow (1987) found it difficult to accept. We would suggest that pseudoautosomal or Y-linkage might be found if selected cases of father-son transmission were investigated, and that the X-linkage for the long arm already found in some families with affective disorders might be associated with those cases showing sex concordance.

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SIR: Certainly the possibility of heterogeneity must not be forgotten. Drs Schiwach & Crocker follow in the confident footsteps of the Lancet leader writer (1987) and Lander (1988) in concluding that it has already been established. But neither must it be too readily conceded. Occam's razor – that the simplest viable solution is to be preferred – is a powerful scientific principle.

The pseudoautosomal hypothesis arose from the counter-Kraepelinian notion that the psychoses are distributed along a continuum (Crow, 1986) rather than existing as two discrete entities. As the Lancet leader pointed out, if psychosis is sometimes sex-linked (e.g. in some affective disorders) and sometimes not, it appears that heterogeneity must be accepted. In resisting that conclusion I was forced to consider a pseudoautosomal locus (Crow, 1987), and having done so realised that it could account for same-sex concordance. This finding has been known, although neglected, in schizophrenia for many years. As far as I am aware it has not been commented on in the affective disorders; but it is present here also (Crow, 1988). The prediction of the pseudoautosomal theory is that it originates when the disease is inherited from the father. This has recently been confirmed in the case of schizophrenia (Crow *et al*, 1989), but not yet tested in the affective disorders.

Drs Shiwach & Crocker's explanation of same-sex concordance on the basis of pseudoautosomal inheritance is misleading in one respect. They are correct in supposing that it will arise when the gene is inherited from the father and not from the mother. The complexity arises from recombination between X and Y chromosomes in male meiosis. As a result of the single crossover that takes place somewhere within the pseudoautosomal region, a gradient of sex linkage exists from the pseudoautosomal limit (where there is sex linkage) to the short arm telomere where there is 50% crossover (i.e. sex linkage is absent). Same sex concordance will arise providing the crossover in either sibling has not occurred proximal to the putative locus. With a locus centromeric in the region (i.e. close to the limit) crossing over will generally be distal, and same-sex concordance will be prominent. With a locus at the telomere (with 50% crossover), concordance by sex will be absent. Therefore the size of the effect gives an indication of the location of the gene – the bigger the effect (assuming that it originates in paternal transmission), the closer the gene is likely to be to the border between pseudoautosomal and sex-specific regions.

But Drs Shiwach & Crocker state that "the obligatory crossover must occur proximally" (perhaps they mean distally) "to the genes in question most of the time (>80%) for the concordance to be observed". While it is true that same-sex concordance could arise as a result of proximal crossover in both siblings, because the rate of crossover in each male meiosis even at the telomere does not exceed 50% (only one of the two chromatids that make up each chromosome is subject to recombination) this will be an infrequent event. Whatever their meaning, Drs Shiwach & Crocker's conclusion is the same as mine – the locus should be close to the border between pseudoautosomal and sex-specific regions.

Drs Shiwach & Crocker draw attention to a number of other ways in which same-sex concordance might arise. Most if not all predict a sex difference such as is absent in schizophrenia and probably also in bipolar affective illness. Therefore, no one of these mechanisms provides a general explanation for transmission of psychosis; nor can they account for concordance by sex except in an unspecified subgroup of cases. A pseudoautosomal locus is compatible with equality of incidence in the two sexes, although it cannot readily explain certain other sex differences, e.g. earlier onset of schizophrenia in

males, the sex ratio in depression. I agree that my attempts to modify the theory in this respect are not entirely successful; but I do not feel compelled to adopt another explanation of concordance by sex while a pseudoautosomal hypothesis still gives some promise of a more general explanation and one which may be applicable to both schizophrenia and affective disorder. Nor am I yet convinced that any of the linkage findings so far provide compelling evidence that genetic loci for psychotic illness are present either on the autosomes or on the long arm of the X. I believe that the problems in the field of psychiatric disorder are such that linkage findings can be regarded as definitive only when there is substantial agreement between two and preferably more independent studies.

For these reasons, encouraged by the counsel of William of Occam (and perhaps also by the example of King Canute) I will adhere to a unitary concept until the tide of heterogeneity flows with greater force. I predict that the genetics of psychosis can be accounted for by changes within the pseudoautosomal region – a one thousandth part of the human genome – and that the findings elsewhere may prove to be irrelevant.

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Elderly eccentrics

SIR: Tantam (*Journal*, December 1988, **153**, 777–782) unfortunately tells us nothing of people aged over 65 years who are apparently eccentric and/or socially isolated.

While there are few (if any) epidemiological data about these subjects, Clark's evocative label 'Diogenes' syndrome' (Clark *et al*, 1975) is immediately recognisable by geriatricians and geropsychiatrists in spite of historical criticism (Cybulska & Rucinski, 1986). When the article by Clark *et al*, appeared, James Williamson, then Professor of Geriatric Medicine in the University of Liverpool, immediately coined the term 'pseudo-Diogenes' syndrome'. By this he meant that the antisocial rejection of help and associated squalor result from a dementing process, whereas Clark reported that all his patients who were formally tested were cognitively competent with "no gross deviation of personality". The distinction continues to be important, particularly when professional carers are asked to act *in loco parentis* for these patients.

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The fear questionnaire

SIR: The recent paper by van Zuuren (*Journal*, November 1988, **153**, 659–662) on construct and discriminant validity, reliability, and layout of the Fear Questionnaire (FQ) with agoraphobic, socially phobic and simple phobic subjects, while it could have contributed to the utility of the instrument for clinical and research purposes, is rampant with errors of omission and is misleading on specific points.

Firstly, in a previous version of the paper (van Zuuren, unpublished), the author noted that the phobics were diagnosed by an experienced psychiatrist, while for the purpose of research in a further stage, the written reports of the clinical interviews that were provided by the psychiatrist were used by a researcher for assigning each patient to any of six phobic categories (three more than included in DSM-III). Each category was concerned with the types of feared and avoided situations. As to agoraphobia, the author noted that its categorisation was based on the researcher's focus on fears of being in public, anonymous situations, and/or being alone. DSM–III requires two additional criteria. In the *Journal* article, however, Dr van Zuuren points out that the patients were categorised according to DSM–III criteria. Clearly, her claim that DSM–III criteria and the guidelines used in her study overlapped to a large extent (van Zuuren, unpublished) can not be upheld. Moreover, the validity of the